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A STUDY OF DIET IN RELATION TO HEALTH. DARK ADAPTATION AS AN INDEX OF ADEQUATE VITAMIN A INTAKE

III.—The Relation of Diet to Rate and Extent of Dark Adaptation

BY

A. M. THOMSON, H. D. GRIFFITH, J. R. MUTCH, D. M. LUBBOCK, E. C. OWEN and G. LOGARAS

THE ROWETT RESEARCH INSTITUTE, ABERDEEN

WHEN this investigation was started (March, 1938), there were three main methods in use for studying dark adaptation as an index of vitamin A intake. The modification of Edmund and Clemmesen's method described by Mutch and Griffith (1937) was being used at the Rowett Research Institute as part of the scheme for an extensive dietary and clinical survey. Meanwhile studies of dark adaptation with the Birch-Hirschfeld photometer had been published by Maitra and Harris (1937) with an estimate of frequency of subnormal dark vision in groups of school children. From America reports had appeared of investigations with the new patented modification of the latter photometer, the biophotometer (Jeans, Blanchard and Zentmire, 1937; Jehgers, 1937) and this method was also being used to assess the incidence of vitamin A deficiency in groups of the population. It appeared desirable, therefore, to determine whether the different methods

already in use, applied to the same subjects, would assess similarly their powers of dark adaptation. Dr. L. J. Harris kindly agreed to co-operate and a series of comparative tests was therefore made. In these, Dr. M. A. Abbasy, from Dr. Harris' laboratory, used the Birch-Hirschfeld photometer and biophotometer, with the assistance of members of the staff of the Rowett Research Institute. Members of the present team used the Mutch-Griffith apparatus and the Rowett adaptometer, described in the second paper of this series (Thomson et al., 1939). It should be noted that the new instrument was then being used simply to estimate the threshold attained by the subject after 15 minutes' dark adaptation, five minutes thereafter being allowed for the test.

Assessments were made on 12 adults (members of staff), 12 adolescent boys from an industrial school and 24 school children from a poor quarter in Aberdeen. After 15 minutes in darkness, each subject was tested on the four instruments in the following order:—Rowett adaptometer; Mutch-Griffith photometer; biophotometer; Birch-Hirschfeld photometer. Tests were made on three consecutive days without vitamin A supplementation and again after an interval (one to 11 days in different cases) during which vitamin A was given as two capsules of halibut liver oil daily.* One of the children was not retested after taking vitamin A, on account of illness.

It is not proposed to present the results in detail. They may be briefly summarised as follows:—of the original 48 cases, 19 were assessed normal and 7 subnormal by all methods. Of 47 retested after taking vitamin A, 38 were assessed normal by all methods. The remaining 22 in the first test, and 9 in the second, were each assessed abnormal by one or more methods, but none of them by all four methods.

The two tests coming first in the series selected many more subjects as " deficient " than did the Birch-Hirschfeld photometer and biophotometer. This suggested that the length of the period in darkness, or dim light, prior to the test might be affecting the results. It was, therefore, decided to investigate the matter more fully on the Rowett adaptometer. A few preliminary tests showed that not all subjects were completely dark adapted in 20 minutes, and that the time required for complete adaptation depended on the antecedent illumination in which the subject had been working. For further clarification of the relationship between previous light conditions and the subsequent rate of dark adaptation, we began to time the course of dark adaptation down the light scale on the adaptometer, following

* We have to thank the Crookes' Laboratories, Ltd., for the gift of ample supplies of halibut liver oil capsules.

various antecedent lights. The development of this work, and a description of the final technique, which gives a result independent of previous light conditions, was given in our second paper (Thomson et al., 1939).

Technical difficulties having been overcome, we investigated the relationship between rate of dark adaptation and vitamin A intake. All the work now to be described was done with the full technique, using the E test object.

Determination of Normal Standards of Dark Adaptation.—At the beginning of this work it was tentatively assumed (*a*) that the vast majority of cases of clinical and subclinical hemeralopia are due to varying degrees of vitamin A deficiency, (*b*) that there is a quantitative correlation between degree of hemeralopia and vitamin A intake and (*c*) that all except a few anomalous and pathological cases of hemeralopia can be cured rapidly by administration of a vitamin A concentrate. These assumptions were founded on much previous work on the subject by many workers, *e.g.*, Jeans, Blanchard and Zentmire (1937), Jehgers (1937), Maitra and Harris (1937), Edmund and Clemmesen (1936), Mutch and Griffith (1937). At this time Palmer and Blumberg (1937), using the biophotometer, and Snelling (1936), using the Birch-Hirschfeld photometer, had shown that results were not reliable nor responses to vitamin A administration consistent, but as the methods were open to criticism on grounds of technique, the physiological concepts behind them were not necessarily invalidated.

With these ideas in mind, we carried out tests on a number of subjects to determine the standards of dark adaptation to be expected in normal subjects, *i.e.*, subjects who habitually took a diet such as is considered not to be deficient in vitamin A. This was done on 53 adults (mainly workers in the Rowett Institute), who were all on a good normal diet, some of whom had been taking halibut liver over long periods and all of whom received one week's supplementation of two capsules of halibut liver oil (17,000 I.U. of vitamin A) daily prior to testing. The average curve obtained and the frequency distribution are presented in Tables I and II. The frequency distribution is based on the "time to aperture 2," which was chosen because, firstly, it represents practically complete adaptation and, secondly, most of those who experienced delay in seeing the test object at aperture 2 gave readings to aperture 4 within the same time range as those who completed adaptation in 14 minutes or less. Repeat tests showed that this delay was not due to lack of practice or of concentration. It should be noted, therefore, that it is inadequate to record only the upper portion of the curve, as the slope of this part seems to bear no constant relation to the form

of the remainder. This point is stressed by Tansley (1939) and has already been discussed in our last paper.

As regards sex differentiation, the above group consisted of 32 males and 21 females. The average for the sexes separately, and the deviations from these averages, are very similar, so that we do not think it necessary to present the data separately.

From the above results, we concluded that subjects who were not deficient in vitamin A might be divided into two groups on the basis of " time to aperture 2 "; the larger of the groups, 80 per cent. of the subjects, reached that aperture in from 7 to 14 minutes and the distribution about the mean was roughly symmetrical. The other group took longer than 14 minutes, and from the differences in the shape of their curves could be considered as being " anomalous " in some way.

As will be seen, further work made this tentative division difficult to retain. It is, however, roughly the basis on which we distinguish between " normal " and " delayed " adaptation. Over 60 per cent. of all subjects fell within the period of 7 to 14 minutes.

Rates of Dark Adaptation in Children on Different Diets.— Following on this, the method was applied in five areas where the Carnegie United Kingdom Trust Dietary Survey was being carried out. Food surveys had been conducted in these areas, so that the vitamin A consumption of the subjects tested could be roughly assessed. The vitamin A figures given in Table I are calculated as the intake per head per day. In three of these areas, an experimental group of children had been given a general dietary supplement for one year previous to the test, the remainder of the surveyed population acting as controls. In the dietary supplements, the main source of vitamin A was halibut liver oil. Milk, cheese, eggs and vegetables also provided part of the supplement of vitamin A. However inaccurate, therefore, the estimates of dietary vitamin A intake from the unsupplemented diets may be, there is no doubt that the vitamin A intake of the experimental children was much higher than that of the controls. Nor is there any doubt that the vitamin A intake of the Rowett adults and public school boys was much above that of the other unsupplemented groups.

Precautions were taken throughout this survey work that the workers did not know whether the subject being tested was from the " fed " or control group. Thus any possibility of influencing the results through preconceived ideas was eliminated.

The first subjects tested were boys in an orphanage whose normal diet contained about 1,000 I.U. of vitamin A per head per day. A proportion of them had received supplements which were calculated to add 5,000 I.U. to this amount daily. Tests

were conducted in July, 1938, when the extra food had been given for six months, and in January, 1939, when it had been given for a year. The average curves obtained and the frequency distributions are shown in Tables I and II. Owing to boys leaving the institution, the groups were not identical at each test, but 24 boys from the fed group and 23 from the control group were tested on both occasions. Table III presents the detailed data for these.

In the interval between these two tests, the method was applied in other areas as follows:—

(1) On 30 children from a community in South Wales, whose average daily intake of vitamin A was approximately 3,000 I.U. per head per day.

(2) On 50 boys from a private boarding school in the North of Scotland. These boys had been maintained for at least a year previously on a first-class diet and in a first-class environment. The vitamin A content of the diet was approximately 6,000 I.U. per head per day, and this was derived chiefly from actual foodstuffs, not from vitamin A concentrates.

(3) On school children in two rural villages in Aberdeenshire, which are five miles apart and similar as regards size of population and type of inhabitant. In one village the children, for a year previously, had received a school meal which contained about 3,500 I.U. of vitamin A per head per day. Their home diet provided about 1,500 I.U. per head per day. The children from the control village had about 2,500 I.U. per head per day, on an average.

(4) In March, 1939, tests were made on 21 " fed " children and 18 " control " children in Dundee. The average home diets of the fed and control groups contained between about 1,000 I.U. and 1,500 I.U. of vitamin A per head per day. The former received a supplement which provided a further 3,500 I.U. or so per head per day.

The data for these tests are presented in Table I as the average curves for each group, and in Table II as the frequency distributions of the " time to aperture 2." All the children tested adapted ultimately to aperture 2 illumination.

It will be seen that it is not the case that slower average curves are associated with lower average vitamin A intakes. Inspection of the data of individuals shows that there is no correspondence between the frequency distributions about the means of the rate of dark adaptation and of vitamin A intake. For reasons of space we are unable to present the detailed data here. In the groups where supplementary feeding was given, no improvement in the standard was obtained. The only exception to this was the summer test in the orphanage, where the " fed " group did significantly better than the control group. This difference was not maintained six months later.

TABLE I—AVERAGE CURVES

GROUP		No. in Group	Average Vit. A intake, per head per day	APERTURE 9	8	7	6	5	4	3	2
				M. S.	M. S.	M. S.	M. S.	M. S.	M. S.	M. S.	M. S.
Rowett Adults - - -		53	Good normal diet (not analysed)	0 51	1 10	2 1	2 53	4 11	5 47	8 44	12 33
Public School - - -		50	6000 I.U.	1 20	2 11	3 23	4 36	6 0	7 45	10 24	13 30
Welsh Group - - -		30	3000 I.U.	1 11	1 44	2 55	3 55	5 34	7 9	9 31	12 58
Aberdeenshire Agriculture Group	Fed - -	33	1500 I.U. +3500 I.U.	2 7	3 9	4 33	5 39	7 13	9 41	13 17	20 4
	Control -	24	2500 I.U.†	1 54	2 54	4 1	5 13	6 39	8 35	12 16	19 56
Dundee Group	Fed - -	21	1000–1500 I.U. +3500 I.U.	1 24	2 18	3 32	4 41	6 11	7 57	10 53	15 54
	Control -	18	1000–1500 I.U.	1 33	2 23	3 49	4 50	6 17	8 21	11 6	16 36
July 1938, Orphanage, January, 1939	Fed - -	45*	1000 I.U. +5000 I.U.	0 59	1 28	2 5	3 17	4 35	5 53	8 35	11 14
	Control -	34*	1000 I.U.	1 9	1 48	2 40	3 41	4 59	6 30	10 4	16 6
	Fed - -	31*	1000 I.U. +5000 I.U.	1 39	2 28	3 48	4 51	6 24	8 6	10 38	13 40
	Control -	37*	1000 I.U.	1 30	2 24	3 38	4 49	7 19	7 55	10 25	13 31

* 24 common to both fed groups, and 23 to both control groups.
† Excluding two cases where the intake is more than double the average this figure becomes 2000.

TABLE II—FREQUENCY DISTRIBUTIONS

GROUP		No. in Group	MINUTES TO APERTURE 2																							
			7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30 or more
Rowett Adults		53	1	2	4	7	17	7	2	3	1	1	2	...	...	2	1	2	...	...	1	...	...	...	...	...
Public School		50	...	...	4	3	6	6	3	7	6	5	3	3	...	2	1	...	...	1	...	...	...	...	...	...
Welsh Group		30	...	...	...	5	6	4	4	1	4	5	...	1	...	...	...	...	...	...	...	...	...	...	...	...
Aberdeenshire Agriculture Group	Fed	33	...	...	1	1	...	1	3	3	3	1	2	1	3	...	2	2	2	1	...	1	2	...	1	3
	Control	24	...	1	...	...	...	1	...	2	1	3	2	1	1	3	2	1	...	...	1	...	2	1	1	1
Dundee Group	Fed	21	...	1	1	...	2	3	...	1	1	3	4	1	...	...	...	2	1	...	...	...	...	...	...	1
	Control	18	...	...	...	...	1	4	1	4	1	...	4	...	2	...	...	...	...	...	...	...	...	...	...	1
July, 1938, Orphanage, January, 1939	Fed	45	...	1	8	9	11	4	7	4	...	...	...	...	...	1	...	...	...	...	...	...	...	...	...	...
	Control	34	...	...	1	3	8	3	3	3	5	1	...	1	...	1	...	...	...	...	...	...	1	1	...	3
	Fed	31	...	...	...	3	7	5	3	3	3	1	2	1	...	1	2	...	...	...	...	...	...	...	...	...
	Control	37	...	...	3	1	2	9	6	6	3	2	2	1	1	...	...	1	...	...	...	...	...	...	...	...
TOTAL		376	1	5	22	32	60	47	32	37	28	22	21	10	7	10	8	8	3	2	2	1	5	2	2	9

TABLE III—DETAILED DATA FOR ORPHANAGE BOYS TESTED TWICE

GROUP	JULY, 1938																JANUARY, 1939													
CONTROL	9		8		7		6		5		4		3		2		9		8		7		6		5		4		3		2	
	M.	S.	M.	S.	M.	S.	M.	S.	M.	S.	M.	S.	M.	S.	M.	S.	M.	S.	M.	S.	M.	S.	M.	S.	M.	S.	M.	S.	M.	S.	M.	S.
W.B. -	1	10	2	5	3	5	4	0	5	5	6	30	8	30	11	15	1	58	3	35	5	15	6	43	7	13	8	48	14	17	18	42
A.T. -	0	35	0	50	1	40	2	25	3	45	5	3	9	5	14	7	1	4	1	44	2	23	3	56	5	8	7	11	10	0	16	56
P.F. -	1	35	2	0	4	35	5	10	6	25	7	25	12	10	16	0	2	8	3	30	5	9	5	47	7	10	8	25	10	13	13	5
H.B. -	0	55	1	30	2	13	3	30	4	35	7	0	11	35	18	15	1	20	2	16	3	25	4	40	5	17	6	34	7	37	9	10
J.K. -	1	30	1	50	3	5	3	40	5	5	7	10	11	20	15	5	0	58	2	50	3	44	3	59	7	23	9	51	14	14	17	40
R. McQ.	1	0	1	15	1	50	2	20	2	55	6	0	7	30	10	55	1	42	2	14	3	15	4	31	5	40	8	19	9	10	11	21
T.G. -	1	0	1	30	1	45	3	45	5	0	5	45	8	15	9	40	1	25	2	25	3	39	4	33	5	44	8	42	10	45	14	30
A.D. -	1	35	2	21	2	55	3	30	4	25	5	20	7	0	9	50	1	3	2	10	3	20	5	30	6	44	8	8	9	48	12	15
G.G. -	0	50	3	25	4	0	4	45	5	45	7	35	24	0	54	0	2	4	3	43	4	42	5	37	7	34	8	31	9	50	13	5
J.T. -	2	30	2	55	3	25	4	0	5	5	8	30	12	0	36	0	1	11	1	55	4	47	5	15	7	32	8	56	10	42	14	45
S.G. -	0	30	1	0	1	40	2	25	2	55	4	10	7	45	11	20	0	24	0	47	1	5	1	32	3	7	4	44	5	43	10	0
I.K. -	1	2	1	45	2	35	3	30	5	5	6	15	8	5	27	20	1	45	3	0	4	40	5	16	6	3	8	22	9	44	12	49
J. McK. -	1	5	2	10	2	50	3	40	5	20	7	25	10	10	14	35	0	40	1	7	2	11	3	38	6	5	7	35	11	20	12	0
A.S. -	1	0	1	25	1	45	2	15	3	30	5	55	8	5	12	20	0	45	1	0	2	15	3	23	4	23	6	5	7	48	12	24
H.F. -	0	45	1	25	2	5	3	40	5	5	6	10	8	45	19	40	1	25	1	50	2	21	4	16	5	29	7	54	11	39	17	15
A.W. -	1	20	2	5	3	30	4	30	6	0	7	20	9	0	14	35	2	7	3	45	5	29	6	29	8	3	9	4	12	40	15	48
D.D. -	1	5	1	20	1	50	3	35	4	50	6	45	9	45	14	25	1	17	2	2	4	6	4	56	6	45	8	31	10	55	13	53
G.P. -	1	5	1	20	1	55	5	15	5	50	6	30	10	40	12	0	1	35	2	44	4	59	6	0	6	22	7	52	11	9	12	15
N.G. -	0	50	1	45	2	15	3	35	4	25	5	30	7	25	15	10	1	45	2	15	3	56	5	6	7	48	8	13	11	7	13	12
A.C. -	1	0	1	30	2	30	3	40	5	0	6	5	8	35	10	50	2	15	3	18	4	30	5	28	7	31	9	29	12	15	13	52
E.B. -	1	20	1	45	4	0	4	45	5	30	6	55	9	25	11	5	2	32	3	47	4	38	5	8	6	57	9	13	9	48	11	38
H.R. -	1	15	1	40	2	15	3	50	6	5	6	45	7	50	11	20	1	11	1	34	2	34	5	21	7	9	7	48	9	0	12	25
E.W. -	2	0	4	35	5	30	6	15	7	35	8	20	9	25	12	45	1	2	1	29	2	31	4	32	6	14	7	16	9	55	11	20

TABLE III—*contd.*

TABLE III—*contd.*

GROUP	JULY, 1938								JANUARY, 1939							
FED	9	8	7	6	5	4	3	2	9	8	7	6	5	4	3	2
	M. S.	M. S.	M. S.	M. S.	M. S.	M. S.	M. S.	M. S.	M. S.	M. S.	M. S.	M. S.	M. S.	M. S.	M. S.	M. S.
G.V. -	1 2	1 27	2 27	3 20	4 56	6 20	8 53	11 12	...	...	...	...	...	...	...	11 30
J.S. -	1 40	2 5	2 45	4 20	5 15	6 20	8 20	10 35	2 53	3 17	5 10	6 10	7 32	8 43	10 21	14 53
R.G. -	1 15	1 45	2 10	3 0	4 40	6 15	7 48	9 45	1 27	2 15	3 41	4 53	6 14	8 33	10 35	13 8
A. McK. -	0 45	1 10	1 35	2 30	4 50	5 55	7 55	9 25	1 7	2 8	4 0	4 42	6 20	7 6	9 18	12 25
M.H. -	0 45	1 10	1 40	2 10	2 55	5 25	6 30	9 30	0 47	1 9	1 56	2 33	4 10	6 45	8 7	9 44
J.S. -	0 45	1 2	1 50	2 45	3 30	5 50	8 30	11 30	1 22	2 7	3 26	4 43	6 7	8 24	12 13	13 15
C.M. -	0 45	1 25	2 0	2 30	4 40	5 30	8 30	13 50	1 23	1 57	3 32	4 55	6 58	7 40	11 50	16 40
J.H. -	0 55	1 20	1 58	3 10	4 55	5 58	7 50	10 20	1 6	2 30	4 45	5 23	7 43	8 58	10 24	11 43
D.D. -	0 55	1 10	1 50	3 15	4 0	5 20	7 15	10 30	1 10	1 38	3 0	3 42	4 33	7 0	10 26	11 13
J.L. -	0 55	1 25	2 20	3 10	4 10	5 40	8 15	13 0	1 40	3 6	4 6	5 28	6 48	8 30	13 9	15 0
W.R. -	1 2	1 28	2 50	3 27	4 58	6 44	9 32	13 30	1 36	2 21	3 50	4 49	6 58	8 42	12 34	15 40
J. Mc.D. -	1 10	1 35	2 20	3 40	4 55	6 35	8 45	14 10	1 27	2 35	3 50	4 42	6 26	7 27	9 58	12 17
E.M. -	0 55	1 25	1 55	2 50	4 30	6 25	10 5	13 55	...	...	...	...	...	...	...	10 35
J.R. -	0 55	1 5	2 15	4 25	5 55	7 30	10 20	13 0	...	...	...	...	...	...	...	21 15
S.G. -	0 55	1 58	2 20	3 55	5 0	6 40	8 55	11 30	1 3	1 41	3 10	3 35	5 20	6 43	8 24	10 7
R.D. -	0 55	1 20	2 5	3 50	4 50	6 0	9 0	10 50	1 5	2 5	2 21	4 9	5 44	6 56	7 18	11 19
H.F. -	0 55	1 15	1 50	2 40	3 17	5 10	8 44	11 20	1 0	2 1	3 7	4 10	6 18	7 1	9 41	11 10
D.W. -	1 0	2 0	3 5	3 35	5 45	7 20	11 0	14 5	1 49	2 58	5 3	5 35	7 23	9 50	13 45	14 8
G.L. -	1 45	2 30	2 55	3 45	6 10	6 45	10 0	13 20	...	...	...	...	...	...	...	11 20
F.C. -	0 55	1 30	2 10	3 50	4 40	5 40	9 35	12 40	1 20	2 33	3 55	5 15	6 45	8 33	10 39	13 7
R.R. -	0 55	1 15	2 10	2 40	3 24	4 15	9 5	12 10	...	...	...	...	...	...	...	11 55
J.W. -	1 10	1 20	2 0	3 25	4 30	5 20	8 35	10 45	1 48	2 5	3 38	4 45	6 20	6 55	11 12	20 48
P.S. -	0 55	1 5	1 30	2 45	4 40	6 55	9 40	11 30	1 16	2 34	3 36	5 18	6 44	8 26	12 40	17 4
A.B. -	0 50	1 50	3 10	4 5	5 0	5 40	9 40	11 30	...	...	...	...	...	...	...	17 53

Inspection of the detailed orphanage results (Table III) shows that the rate of adaptation in certain individuals changed markedly in the six months between the July and January tests, e.g., G.G., J.T., I.K., J.R., J.W. These changes did not correspond to any known change in the diet or environment. It is noteworthy that the greatest changes are for the better. As a number of these cases were tested twice on each occasion, with excellent agreement between the results, the improvement does not appear to have been due to practice.

Effect of Vitamin A Administration in Individual Cases.—Two groups of children at the orphanage who gave slow curves were intensively treated with vitamin A concentrate and retested at intervals. The first group (four boys) had been on the basal diet for at least one year previously. The second group (two girls and one boy) had been on the supplemented diet for a year. A control group of 5 boys was tested at intervals without receiving any medication. In order that the question of the vitamin A potency of the halibut liver oil might not arise, half the children were given halibut liver oil (18,000 I.U. of vitamin A daily) and half avoleum (12,000 I.U. vitamin A daily).

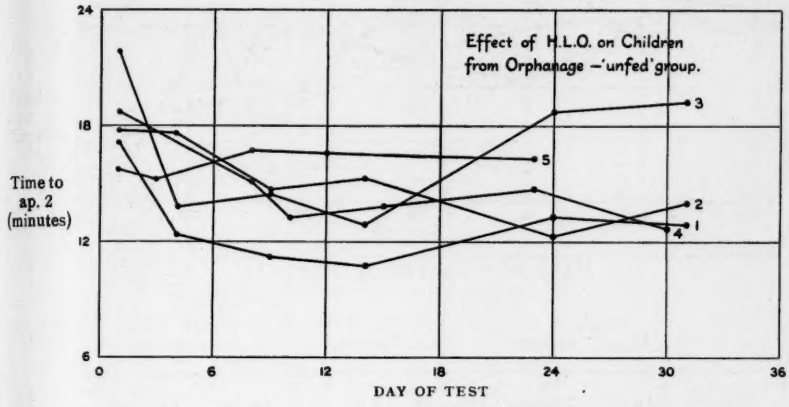
The results are summarised in Graphs 1, 2 and 3, plotted as " time to aperture 2 " against the day of test. It will be seen that no consistent improvement was produced by the vitamin A. Of exceptional interest, however, is the dramatic improvement in two cases in group 2 (Graph 2) which occurred after the ninth day of supplementation. If this improvement was due to vitamin A, the question of a critical dose or of cumulative effect arises. This should be considered in connection with questions of absorption of the vitamin (see discussion).

A similar experiment was carried out for three weeks on four children in Aberdeen. These had a preliminary test; then they were given two capsules of halibut liver oil (about 16,000 I.U. of vitamin A) daily and retested at intervals. The data of this experiment are not complete owing to domestic disturbances in the families concerned. The results are shown in Graph 4 and show fluctuations similar to those obtained in the orphanage. One child in this series should receive special mention (curve marked G.K.). He had been tested six months previously, in summer, during the experimental work on technique, and had given very slow curves on several occasions. The improvement which his performance underwent during the next six months is parallel to one or two cases in Table III. Here, also, there was no obvious change in diet or surroundings, other than the treatment with halibut liver oil which he had during the tests six months earlier, which might account for the change in rate of dark adaptation.

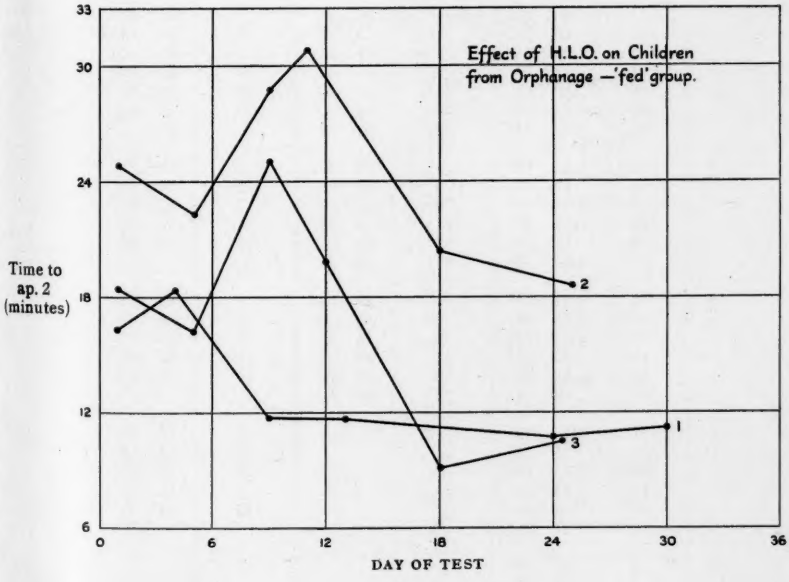
In addition to these data, there are the cases of certain workers at the Rowett Institute who have consistently given very slow

curves in spite of a good diet and vitamin A supplementation. It has been noted and verified that they show marked changes in rate of adaptation from one time to another which we are unable to assign to any dietary or environmental cause. (But see also page 719.)

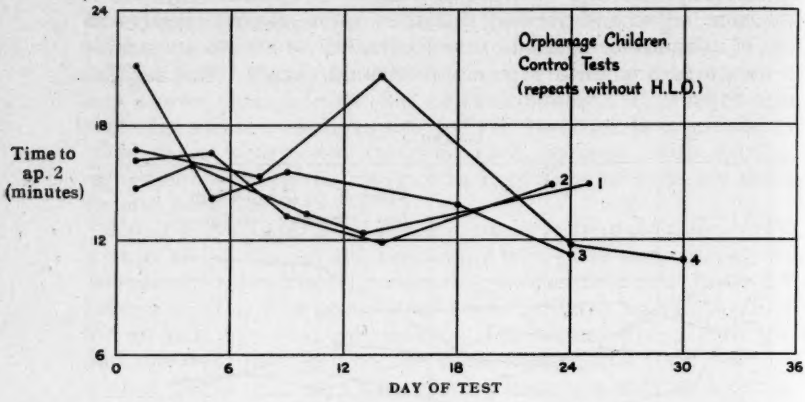
GRAPH 1



GRAPH 2.



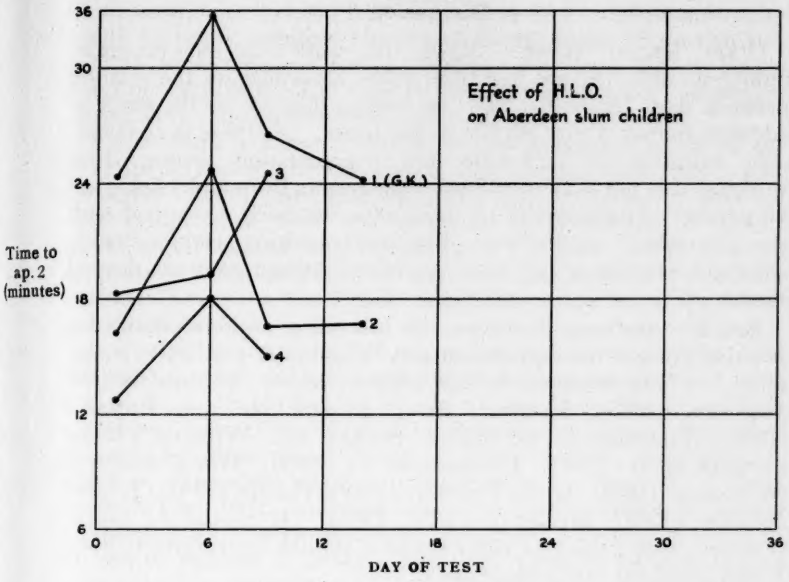
GRAPH 3.



DATA FOR GRAPHS 1, 2 AND 3

	GRAPH I "Unfed" Group		GRAPH II "Fed" Group		GRAPH III Control Group	
Curve No.	Day of test	Time to Ap. 2	Day of test	Time to Ap. 2	Day of test	Time to Ap. 2
		M. S.		M. S.		M. S.
1	1	17 15	1	16 20	1	14 45
	4	12 23	4	18 23	4	16 0
	9	11 17	9	11 43	10	13 15
	14	10 45	13	11 20	14	12 20
	24	13 19	24	10 45	25	14 58
	31	12 52	30	11 12	...	...
2	1	17 40	1	24 55	1	16 23
	4	17 37	5	22 26	5	16 32
	9	14 38	9	28 50	9	13 11
	14	14 47	11	30 47	14	11 52
	24	12 11	18	20 26	23	14 57
	31	14 0	25	18 34	...	...
3	1	21 57	1	18 24	1	21 15
	4	13 48	5	16 7	5	14 10
	9	14 35	9	24 54	9	15 34
	14	12 53	12	19 38	18	12 42
	24	18 34	18	9 10	24	11 20
	31	19 4	25	10 35	...	...
4	1	18 42	...	...	1	16 56
	8	15 3	...	...	8	15 4
	10	13 25	...	...	14	20 35
	15	14 44	...	...	24	11 39
	23	14 46	...	...	30	11 0
	30	12 35	...	...	...	...
5	1	15 48	...	...	...	...
	3	15 15	...	...	...	...
	8	16 35	...	...	...	...
	12	16 30	...	...	...	...
	23	16 18	...	...	...	...

GRAPH 4.



DATA FOR GRAPH 4

Curve No.	Day of test	Time to Ap. 2
		M. S.
1	1	24 27
(G.K.)	6	32 50
	9	26 32
	14	24 4
2	1	16 3
	6	24 40
	9	16 32
	14	16 54
3	1	18 15
	6	19 25
	9	24 40
4	1	12 37
	6	18 8
	9	15 0

Discussion

Other Recent Work.—While the work was in progress, numerous observations had been made elsewhere on the relation between dark adaptation and the normal diet, or on the effect of adding vitamin A concentrate to the latter. As there is considerable variation in technique and interpretation among these workers, it is not easy to analyse their results from a physiological viewpoint. The majority of them have not been concerned with the physiology of the test, but were working empirically to ascertain whether or not some particular method gave the desired results.

Broadly speaking, however, the following workers obtained a positive correlation between dietary vitamin A and dark adaptation, or improvement on the administration of concentrates: Frandsen (1937), Toverud (1937), Friderichsen and Edmund (1937), Youmans et al. (1937), Booher and Williams (1938), Corlette et al. (1938), Caussade et al. (1938), Gridgeman and Wilkinson (1938), Groth-Petersen (1938), Haines (1938), Juhász-Schäffer (1938), McKenzie (1938, 1939). It should be noted, however, that Juhász-Schäffer found a similar improvement when wheat germ oil was administered.

Other workers (Poulsen (1937), Snelling (1938), Gantzel (1938), Frazier and Li (1938), Isaacs, Jung and Ivy (1938) and Palmer (1938)) found no correlation between dietary vitamin A and dark adaptation, or no consistent improvement on administration of vitamin A.

Staz (1937), Schuck and Miller (1938), Vanzant (1938) and Kentgens (1938) obtained equivocal results. Vanzant stressed the technical difficulties of the method. Staz studied the dark adaptation of 200 Rand miners, about 20 per cent. of whom showed delay in the first test. When these were retested after seven months 20 per cent. were still defective, but only 4 per cent. were defective at both tests.

Booher et al. (1939), Hecht and Mandelbaum (1939), Wald, Jehgers and Arminio (1938), Jehgers (1937), and Pett (1938) have observed the effect on dark adaptation of an experimental diet low in vitamin A, using various techniques. They all report diminished rate of dark adaptation or a raised threshold after a specific time, the first effects being observed after a period on the diet which varied from 1 day (Hecht and Mandelbaum, 1939) to 124 days (Booher et al., 1939).

There is also considerable doubt about the time required for a " cure " by administration of vitamin A. Thus Wald, Jehgers

and Arminio* obtained a response in about 30 minutes by oral administration of 100,000 I.U. in one dose and complete normality within 2½ hours, whereas Hecht and Mandelbaum found that two months were required for a complete cure and that a single injection of 100,000 I.U. during the period of slow adaptation caused very little and very transient change.

The attempt has been made by certain workers to correlate the vitamin A content of the blood and rate of dark adaptation. Lindqvist (1938) and Juhász-Schäffer (1938) obtained positive results, but these were not confirmed by Baum and McCoord (1939) and Pies and Wendt (1939). Kentgens (1938) found a correlation in the majority of his cases, but showed that certain persons have subnormal dark adaptation even when the blood vitamin A is normal.

It should be noted that, of the above workers, those who used the same instruments are in considerable disagreement as to what constitutes a reliable technique. In no case have they tested their techniques adequately in order to determine the extent and effect of variables other than vitamin A administration, especially the effect of antecedent light. It appears to us that all of these methods must have considerable uncontrolled variables, the extent of which has not been accurately compared with that believed to be due to vitamin A intake. For these reasons, we believe that both positive and negative results should be accepted with reserve.

Effect of Colour.—One point in technique has been examined by us since finishing the survey work. Our method is possibly the only one in which white light was used throughout the study. The Edmund and Clemmesen method and its modification used Tscherning " neutral " glasses, which are reported as blue by Vraa-Jensen (1936).† The Birch-Hirschfeld photometer and the method used by Wald, Jehgers and Arminio employ " neutral " wedges to reduce the light; the biophotometer technique, reducing the light by means of a rheostat, may change the quality of the light at low illuminations; and the method described by Hecht and Shlaer (1938) employs deep violet light.

In order to test whether our negative results might be due to the use of white light in the photometer, a violet filter was inserted behind the diaphragm (Wratten filters 35 and 64), providing a

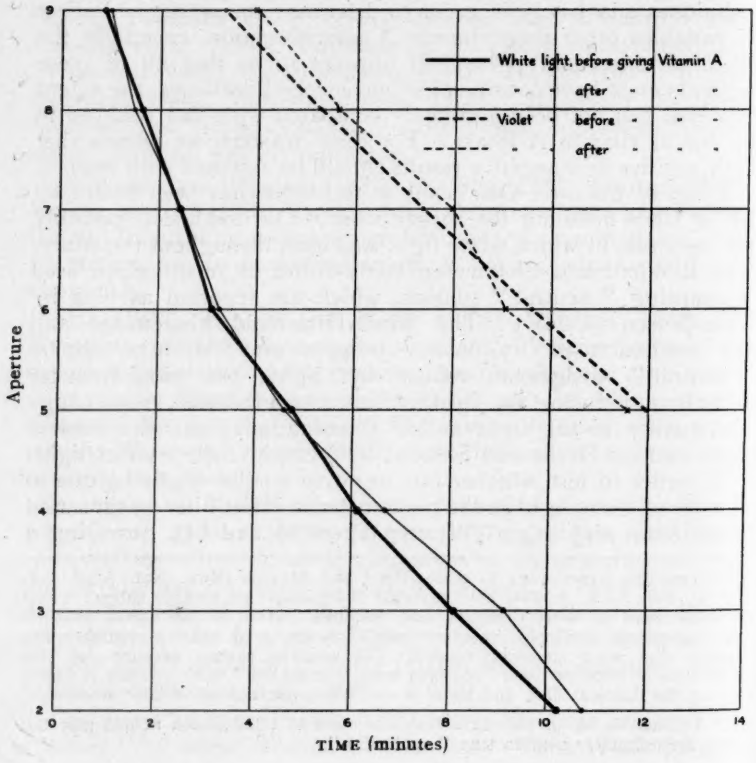
* Since this paper went to press, Wald and Stevens (Proc. Nat. Acad. Sci. (1939), Vol. XXV, p. 344) have reported observations on another subject which confirm those of Wald, Jehgers, and Arminio; but it is also stated that no night-blindness developed in about half of a group of subjects (number not given) who were similarly treated. The authors cannot account for this difference in response, as all subjects were " saturated " with vitamin A before taking the deficient diet, and hence it was not a question of variable reserves.

† An analysis by us showed a low maximum of transmission at 520 mμ; but they are extremely near to true " neutrality."

cut off at 480mμ, corresponding to the quality of light employed by Hecht and Shlaer. In order to obtain sufficient light at the test object a 24 watt 6 volt car headlamp bulb was used in place of the standard bulb, and run from an accumulator. There was no voltage control, so the experimental error was wider than with the standard apparatus, but we did not think it large enough to interfere with the purpose of the experiment. The U test object was used.

Five adults on an adequate diet were tested with white light and immediately afterwards with violet. They were then given 17,000 I.U. of vitamin A daily, as halibut liver oil, for seven to 10 days, and retested. The average curves are presented in Graph 5. From these results it was concluded that aperture 5, using the violet light, was roughly equivalent to aperture 2 on

GRAPH 5.—SAME SUBJECTS, TESTED WITH AND WITHOUT VIOLET FILTER.



DATA FOR GRAPH 5

		WHITE LIGHT								VIOLET LIGHT					
		9	8	7	6	5	4	3	2	9	8	7	6	5	
		m. s.	m. s.	m. s.	m. s.	m. s.	m. s.	m. s.	m. s.	m. s.	m. s.	m. s.	m. s.	m. s.	
I.D.	27/6/39	0 55	1 48	2 8	2 58	5 5	6 10	8 33	10 22	5 12	6 4	7 47	9 44	1 42	
	5/7/39	0 57	1 50	3 24	3 50	4 42	6 28	8 48	12 27	4 23	6 5	8 10	10 10	13 15	17,000 I.U. Vitamin A daily since previous test
A.M.T	27/6/39	0 24	0 58	1 30	2 33	4 7	5 50	7 35	9 53	1 40	2 10	3 55	7 48	9 58	
	5/7/39	0 30	0 42	1 17	1 37	3 40	5 27	8 5	8 55	2 0	4 8	5 8	6 45	9 5	17,000 I.U. Vitamin A daily since previous test
E.C.O.	28/6/39	0 35	1 7	1 24	1 50	4 14	5 11	7 51	8 48	3 14	4 32	6 55	8 45	10 44	
	6/7/39	0 28	0 48	1 3	2 13	4 2	6 21	8 16	9 35	3 2	4 56	6 13	8 8	11 7	17,000 I.U. Vitamin A daily since previous test
J.L.	30/6/39	1 31	2 57	4 55	5 46	7 10	7 55	10 10	12 18	2 25	7 25	10 45	12 15	12 42	
	10/7/39	1 40	2 40	4 5	4 35	6 25	8 5	12 45	13 20	5 30	7 00	7 50	10 40	12 50	17,000 I.U. Vitamin A daily since previous test
E.H.	30/6/39	0 44	1 11	1 56	2 31	3 1	5 29	6 46	9 40	4 40	5 55	7 22	9 26	12 50	
	7/7/39	0 53	1 18	1 57	3 20	4 28	6 58	7 49	9 12	4 28	5 55	7 30	9 43	11 45	17,000 I.U. Vitamin A daily since previous test
Averages		0 51	1 36	2 23	3 8	4 43	6 6	8 5	10 12	3 26	5 13	7 21	9 36	11 59	Before Vitamin A administration
		0 54	1 28	2 21	3 11	4 39	6 40	9 9	10 42	3 53	5 37	6 57	9 5	11 36	After Vitamin A administration

TABLE IV—EFFECT OF HALIBUT LIVER OIL ON CHILDREN, USING VIOLET LIGHT FOR TESTS

		9	8	7	6	5	
		M. S.	M. S.	M. S.	M. S.	M. S.	
C.B. - -	12/7/39	4 35	6 30	7 30	12 25	19 20	
	19/7/39	5 12	6 55	7 50	9 30	16 50	17,000 I.U. Vitamin A daily since previous test.
	26/7/39	5 24	7 55	8 42	9 15	17 10	" " " " " " " "
M.B. - -	12/7/39	4 50	7 7	9 20	10 40	14 20	
	19/7/39	4 35	6 33	7 50	11 0	19 30	" " " " " " " "
	26/7/39	2 55	5 0	6 25	7 45	14 5	" " " " " " " "
J.A. - -	12/7/39	7 55	10 8	12 4	16 14	18 37	
	19/7/39	3 20	8 40	10 55	12 30	29 5	" " " " " " " "
	26/7/39	5 55	8 15	9 45	13 20	16 25	" " " " " " " "
M.M. - -	13/7/39	5 30	7 0	8 3	8 55	11 20	
	17/7/39	6 20	6 55	10 0	13 25	14 17	" " " " " " " "
	24/7/39	5 0	6 40	7 50	10 2	14 42	" " " " " " " "
W.M. - -	13/7/39	6 45	7 55	8 55	11 35	19 0	
	17/7/39	6 12	7 18	8 30	10 30	17 58	" " " " " " " "
	24/7/39	5 7	6 40	7 48	9 45	16 30	" " " " " " " "
C.S. - -	14/7/39	2 25	6 51	8 55	12 17	17 47	
	20/7/39	6 50	8 15	9 25	11 35	12 40	" " " " " " " "
	27/7/39	6 15	6 50	7 57	9 25	11 15	" " " " " " " "
G.B. - -	14/7/39	6 50	7 57	9 17	13 4	14 5	
	20/7/39	6 15	7 22	8 30	9 55	16 10	" " " " " " " "
	27/7/39	1 0	3 35	4 30	6 25	7 15	" " " " " " " "
S.B. - -	14/7/39	3 24	6 55	10 12	12 8	13 10	
	20/7/39	6 25	12 20	13 35	14 20	18 20	" " " " " " " "
	27/7/39	0 25	0 50	7 25	7 55	10 45	" " " " " " " "
M.B. - -	18/7/39	2 35	5 10	6 55	7 25	14 10	
	25/7/39	4 24	5 20	6 40	9 35	16 25	" " " " " " " "
R.M. - -	18/7/39	6 45	7 15	7 40	8 20	17 17	
	25/7/39	4 55	6 12	8 18	9 50	11 15	" " " " " " " "
S.H. - -	13/7/39	6 50	8 45	10 35	13 46	17 57	
	17/7/39	5 42	8 32	12 10	20 32	21 47	" " " " " " " "

the standard apparatus. Direct measurements of illumination were not made.

Following on this, 12 children from a slum clearance area in Aberdeen were tested with violet light, then given two capsules of halibut liver oil daily for varying intervals, and retested twice during the dosage period (in some cases once). The testing of one child had to be abandoned owing to lack of co-operation. The results for the remainder are shown in Table IV.

It will be seen that there seems to be no very significant difference between the results on white light and on violet light.

Sources of Error.—Apart from the technical differences and errors which have confused the study of this problem, many other difficulties arise to complicate the issue.

The estimation of the amount of vitamin A or its precursors in foodstuffs has not yet reached a high degree of precision; published results for any one foodstuff show a wide range of variation, and it is not possible to be certain that published results are valid for the particular foods in any one diet. In experimental studies in which large doses of concentrates are given, this is not of importance, but it is of importance when attempts are made to correlate the vitamin A or carotene content of natural foodstuffs with dark adaptation.

Absorption and Utilisation.—It is generally held that preformed vitamin A and its precursors are absorbed into the portal circulation and that the liver acts as a store in which conversion of precursors to vitamin A takes place. It has been found that preformed vitamin A is almost completely absorbed from the intestine (Wendt (1937), Wilson et al. (1937); De (1937)) but that only half or less than half of the carotenoids may be absorbed (Wilson et al.; De; Van Eekelen and Pannevis, (1938); Clausen and McCoord (1938)). The absorption of carotene depends upon the simultaneous presence in the intestine of a suitable solvent (Van Eekelen and Pannevis, Wilson et al., De) and the loss of both precursors and of vitamin A in the faeces may be increased by the presence of other substances, such as mineral oil (Andersen, 1938).

Storage.—Little is known about the storage of vitamin A in the human subject, but it is a possibility that fluctuations in response to the administration of vitamin A and to diets low in vitamin A may be due to variable stores or storage capacity. Moore (1937) estimated the vitamin A reserves in 1,000 adult livers and found that these varied greatly in various pathological states. Ellison and Moore (1937) estimated the reserves at

autopsy of the livers of children under 15 with similar results. Work on animals does not give much more information about factors influencing storage. However, Davies and Moore (1937) brought forward evidence that vitamin A reserves in the rat are influenced by previous diet. Chevallier, Choron and Espy (1936) found a seasonal fluctuation of liver reserves in guinea pigs. Thorbjarnarson and Drummond (1938) claimed that storage in the rat was maximal when the diet contained much fat and that choline depleted these stores. Their results, however, were not substantiated by Lease and Steenbock (1939).

Rôle of Vitamin A in Light Perception.—Since the experiments of Fridericia and Holm (1925) who showed that dark adaptation is accompanied by regeneration of visual purple in the retina, it has usually been considered that retinal sensitivity is a simple function of visual purple concentration in the retina. Hecht had shown (1920) that the retinal sensitivity curve of the human subject fits the theoretical curve of a bimolecular reaction and it seemed probable that the bleaching and regeneration of visual purple was due to a reversible bimolecular reaction. The work of Wald (1934) further suggested that vitamin A was one of the breakdown products of visual purple during bleaching and a visual purple —visual yellow—vitamin A cycle was postulated and formed a physiological background to clinical observations that subjective night blindness may be cured by vitamin A concentrates.

Recently, however, there have been critics of this hypothesis. Krause and Sidwell (1938) found no evidence of vitamin A, or substances of a carotenoid nature in the decomposition products of ox visual purple, and suggest that Wald's hypothesis was based on a non-specific colour reaction. Granit et al. (1939), in a series of well controlled experiments on frogs and cats, showed that retinal sensitivity, as measured by the electrical response, is not a simple function of visual purple regeneration, and that the progress of the latter does not fit Hecht's theoretical bimolecular curve. In the cat, the electrical response may be absent when as much as 40 per cent. of the maximum concentration of visual purple is present in the retina.

The Rôle of Substances Other than Vitamin A in Dark Adaptation.—Recently it has been claimed by Stewart (1939) that, whereas dark adaptation bore no relation to vitamin A intake, and administration of concentrates to " slow " subjects had no effect, the addition of large doses of ascorbic acid with the vitamin A caused an immediate response. Kimble and Gordon (1939) claim

that subjects who do not improve under intensive vitamin A administration respond to lactoflavin or to ascorbic acid.†

We find it difficult to support these results for the reason that in our survey reported above general dietary supplements were given, including vitamin C and lactoflavin (in natural foodstuffs). Furthermore, vitamin C saturation tests were made by Dr. J. Pemberton on 62 boys at the orphanage, on 50 of whom hemeralopia tests were also made. The saturation tests showed a complete cleavage between "fed" and "control" boys. Those in the "fed" group were "saturated" with vitamin C in the sense that a marked increase in urinary excretion followed administration of a test dose of ascorbic acid. The controls gave no response and a subgroup of them showed an average deficit of about 1 g. of ascorbic acid. There is no such division in the dark adaptation of the two groups of boys.

Hemeralopia in Pathological Conditions.—It has long been known that clinical night blindness may be associated with icteric conditions. This may be due to depletion of liver stores, or to solution of the visual purple in the presence of bile salts in the blood and its removal from the retina. Haig et al. (1938) report cure of hemeralopia in two of their cases of alcoholic cirrhosis by very high doses of vitamin A by mouth. Bushke (1937) obtained similar results.

Ezickson and Feldman (1937) describe severe hemeralopia in cases of urolithiasis which was not curable by vitamin A administration and postulate a failure of absorption or utilisation rather than a dietary deficiency.

Wohl and Feldman (1939) and Zaffke (1939) find hemeralopia to be associated with hyperthyroidism.

Certain other causes of hemeralopia are known. Thus Duke-Elder (1932) says that clinical night blindness may occur in the following conditions, in addition to vitamin A deficiency: diseases of the eye; congenital and hereditary conditions; pathological changes in the liver; and in association with neurasthenic and functional symptoms where pathological changes and nutritional disturbances are absent.

† Since this paper went to press we have received a paper by Pock-Steen (Geneesk. Tijdschr. Nederl.-Indië (1939), Vol. LXXIX, p. 1986) describing a condition in sprue patients characterised by "twilight blindness," dazzle in bright light, disturbances of accommodation and other abnormalities. There is no response in these cases to vitamin A, but treatment of the sprue by injection of lactoflavin cures all the ocular symptoms. To explain the results the theory is advanced that lactoflavin is the precursor of visual yellow; that visual yellow is the precursor of visual purple, and requires for conversion to visual purple an enzyme and an activator which is vitamin A. Hence, the author says, vitamin A deficiency slows the rate of dark adaptation but does not alter the threshold. Deficiency of lactoflavin (dietary or conditioned, as in sprue) means actual pigment deficiency and may therefore interfere with the extent of adaptation.

Among conditions causing hemeralopia not due to vitamin A deficiency retinitis pigmentosa has long been quoted. But recently some doubt has been cast on this view. Josephson and Freiberger (1937) and Tscherkes (1938) claim to have cured the hemeralopia of retinitis pigmentosa by injection of vitamin A.

There is also a possibility that severe deficiency in childhood may result in permanent hemeralopia. With reference to Hart and Guilbert's observations on domestic animals, Tansley (1939) says that " if the deficiency is allowed to become severe enough to affect the rod structure, the resultant night blindness is, in fact, incurable."

Clinical Night Blindness.—It has long been known that subjective night blindness may frequently be cured by liver or liver oils. More recent confirmation of this observation is given by Fisher (1938) and Vaillant and Gillis (1939).

It appears less certain that hemeralopia is an essential or early part of the vitamin A deficiency syndrome. Thus Ayuyao (1937) describing 393 cases of xerophthalmia in children says that only 44 were night blind, while Sweet and K'ang (1935) found only 50 cases of subjective night blindness in 203 cases of xerophthalmia in adults. Conversely, Aykroyd (1930) quotes Pillat's (1929) observation that of 90 Chinese soldiers complaining of night blindness only 49 showed eye lesions such as Bitot's spots, xerosis or keratomalacia. Aykroyd states that, in Labrador fishermen, night blindness occurs in the majority suddenly and in a severe form and in persons showing no other detectable signs of disease referable to vitamin A deficiency. It is cured, temporarily, within 24 hours, by a single dose of 1-2 oz. crude cod-liver oil. This contrasts oddly with the enormous doses and lengthy time required by Hecht and Mandelbaum (1939) in their four subjects on a diet of low vitamin A content, but it is not possible to draw any conclusions on the extent of cure in Aykroyd's cases except that subjective symptoms disappeared.

It is of interest to note that Aykroyd was unable to determine whether the night blind Labrador fisherman in the dark slowly adapts to the normal threshold. " In practice, a night blind individual does not linger in the dark. . . ." But that a significant degree of dark adaptation did occur is proved by the custom of bandaging one eye during the day so that it could be used at night.

The conclusions of Frazier and Li (1938) are of great interest as they appear to be the only workers who have measured hemeralopia (by the Birch-Hirschfeld method) on subjects who suffered from obvious clinical manifestations of vitamin A deficiency. They do not give full data, but some sentences may

be quoted from their discussion of the subject. " To assume, as others have done, that loss of dark adaptation is invariably present in states of vitamin A deficiency, and that it is a forerunner of other more severe manifestations of the disease is unwarranted. Clinical experience with well-differentiated cases does not support this view. Cases of vitamin A deficiency present themselves without ocular changes. . . . At present the sources of error attending the clinical application of photometry are so many that future developments in instruments and technique must be awaited before dependence can be placed on the data from this source."

Our own observations on subjectively night blind subjects are limited to two adults, but this does not exclude the possibility that there were others equally bad who were not conscious of the condition. Modern conditions of lighting make it difficult to discover hemeralopia. One of these adults remained night blind for months in spite of high doses of halibut liver oil, then suddenly became normal, but unfortunately under uncontrolled conditions which make it doubtful if the cause was vitamin A administration. He did not take any vitamin A concentrates for four months after the " cure " was discovered but did not change appreciably from his new level of dark adaptation.

The other subject, who complained of difficulty in seeing in the dark, and in driving a car at night, was having a good diet, and had been taking two capsules of halibut liver oil (17,000 I.U. vitamin A) daily for 1½ years previously, except during the five weeks prior to her first test. At this time her rate of adaptation was so slow that the observations were not completed. After this test she took halibut liver oil again for seven weeks, which produced a significant improvement, but not a " dramatic " one. For the next week she took 100,000 I.U. of vitamin A daily (as " Vitamin A Oral "—Crookes), returning after that to halibut liver oil. The high dosage produced a marked improvement, but there was a slight relapse three days after returning to halibut liver oil. Finally 100,000 I.U. of vitamin A were injected intramuscularly, and a test was made 17 hours later. On this occasion her performance was completely normal.* The course of her power of dark adaptation is shown in Table V and in Graphs 6 and 7.

We do not propose to comment on these results, except to say that it seems that the hemeralopia in this subject was not due to any *dietary* deficiency of vitamin A. Nor was it due to any known disease or abnormality.

* Owing to the outbreak of war, observations were discontinued, but it is of interest that this subject reported that the " black-out " caused her no unusual inconvenience, and that she was able to go about at night without trouble.

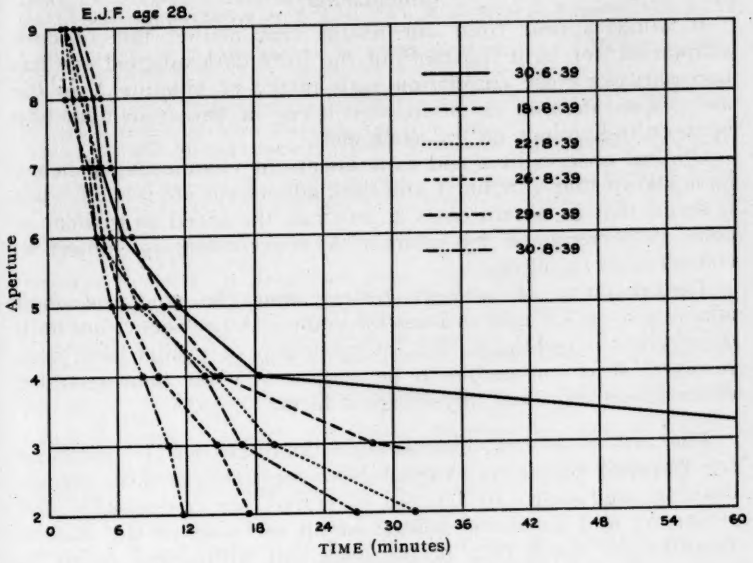
TABLE V

(DATA FOR GRAPHS 6 AND 7)—EFFECT OF VITAMIN A ON A NIGHT BLIND SUBJECT

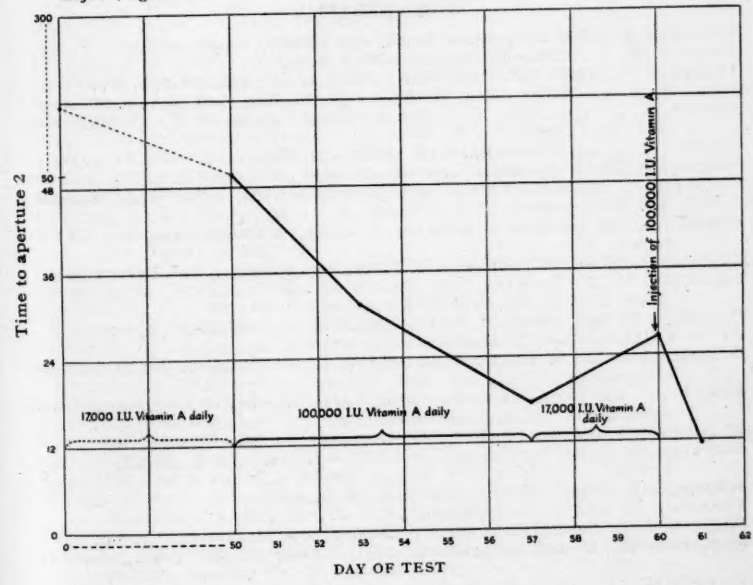
E. J. F., aged 28 years.

	9		8		7		6		5		4		3		2		
	M.	S.	M.	S.	M.	S.	M.	S.	M.	S.	M.	S.	M.	S.	M.	S.	
30/6/39	2	35	4	3	4	43	6	38	11	25	18	20	>60	0	...		
18/8/39	2	47	4	25	5	40	7	5	8	4	14	55	28	0	>30	0	17,000 I.U. Vitamin A daily since previous test.
22/8/39	1	48	3	0	4	23	5	24	7	52	14	40	19	26	31	25	100,000 ,, ,, ,, ,, ,, ,, ,,
26/8/39	1	50	3	25	4	0	4	44	6	30	9	22	14	24	17	20	100,000 ,, ,, ,, ,, ,, ,, ,,
29/8/39	1	10	1	31	3	50	5	10	8	17	13	30	16	32	26	10	17.000 ,, ,, ,, ,, ,, ,, ,,
30/8/39	1	20	2	5	3	15	4	42	5	55	8	7	10	32	11	45	100,000 ,, ,, ,, injected 17 hours before test.

GRAPH 6.



E.J.F., aged 28. GRAPH 7.


Time to aperture 2
17000 I.U. Vitamin A daily
100,000 I.U. Vitamin A daily
17,000 I.U. Vitamin A daily
Injection of 100,000 I.U. Vitamin A
DAY OF TEST

Conclusions

It would appear from our results that neither rate of dark adaptation nor light threshold of the fully dark adapted eye has necessarily a close correlation with intake of vitamin A *in the diet*. Considerable variation may occur in one individual and between individuals on the same diet.

Clinical observations and experiments in vitamin A deficiency have shown that vitamin A and dark adaptation are related. But it seems that in certain cases at any rate the speed and extent of cure of hemeralopia by vitamin A concentrates is subject to considerable variation.

The majority of workers believe that the study of dark adaptation can be used as a test for vitamin A deficiency, but until differences in technique and interpretation of results have been resolved, it is impossible to be certain how far their recorded observations represent physiological facts.

The authors wish to express their thanks to Dr. I. Leitch, of the Imperial Bureau of Animal Nutrition for invaluable advice, criticism and help; to Dr. L. J. Harris for co-operation and criticism; and to many colleagues on the staff of the Rowett Institute for much help in the tests and willingness to act as subjects.

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MACULAR COLOBOMA: HISTOLOGICAL REPORT

BY

ARNOLD SORSBY AND JOHN O. OLIVER

LONDON

THE literature on macular coloboma contains six histological reports. With the exception of one case—that of Rintelen reported in abstract—none is free from objection and none barring the doubtful exception of Deyl's case and the inadmissible case of Janku, refers to a case observed clinically.

(1) Bock (1885). This report concerns the accidental discovery of ectasia at the posterior pole of the two eyes in a man who died, aged 32 years, from pneumonia. No clinical details were available.

(2) Deyl (1898). In a boy who died, aged 5 years, there was hydrocephalus and cleft palate. Clinically there had been observed pale discs in both eyes and a central non-excavated lesion 5 D.D. wide in the left eye; in between this lesion and the disc there was a pale red area with greyish lesions containing vessels.

(3) Van Duyse (1898). In this case a cyclopean eye with two lateral (macular) colobomata forms the basis of the report.

(4) Parsons and Coats (1906). In a female child there was observed at birth an orbital swelling which ultimately led to the death of the child after operation at 9 months. Clinically the right eye was smaller than the left and showed coloboma of the optic nerve, together with other fundus abnormalities " difficult to examine, and the interpretation . . . also difficult." Post-mortem the orbital tumour proved to be an encephalocele, growing from a highly abnormal brain, whilst the eye defects consisted of (1) a cystic bulging on the nasal side of the disc; (2) a large coloboma of the nerve entrance, and (3) " a defect of pigment epithelium in the macular region corresponding with the white patch seen with the ophthalmoscope in this situation; " the fovea itself was intact.

(5) Janku (1923). This study dealt with the eyes of a hydrocephalic boy, aged 11 months [?16 months]. The brain was not examined histologically, and the eyes were studied because Janku considered they showed macular colobomata. Widespread inflammatory reactions were found and parasytic cysts 14 x 22μ to 24 x 30μ were present. Janku held that in his case an inflammatory lesion of the choroid leading to congenital macular coloboma had been set up by intra-uterine infection with a parasite. This case must now be regarded as inadmissible. Apart from the fact that clinically the diagnosis of coloboma is doubtful, the recent study by Wolf and Cowen has established a distinct

clinical entity—encephalitozoic encephalomyelitis—a widespread neurological affection caused by intra-uterine infection by a protozoon. Janku's case is regarded by them as the first recorded instance of this affection. That ocular complications are not an essential feature of this affection is suggested by their reference to another case report.

(6) Rintelen (1934). From the brief report available it is not clear whether the condition was observed clinically. Histologically all the layers at the site of the coloboma were thinned. The choroid was either completely absent or present as a thin layer of pigmented connective tissue; the sclera was reduced to one-third of its thickness; the pigment layer of the retina was missing and at the margins of the coloboma the retina formed an arch. Over the coloboma, only the innermost layers of the retina could be made out. There was no evidence of any inflammatory reaction, and Rintelen regarded failure of development of the pigment layer as the primary fault, the choroidal defect as a secondary feature and the changes in the sclera and retina as the consequences of the choroidal defect.

In addition to these six reports there is a clinical and histological observation by Wexler and Last of coloboma of the optic disc in a (unilaterally) highly myopic eye which also showed changes at the macula, regarded by the authors as probably myopic in origin rather than of the type of congenital coloboma. The retina and choroid over the macular area were poorly developed, laminated fibres of the supra-choroidea appeared to have replaced the choroid for the most part.

Apart from these observations on human eyes there are also the histological findings reported by Hess for the right eye of a rabbit, and by Zimmermann for the left eye of a dog.

These anatomical studies of doubtful material do not go beyond the finding of absence to varying degrees of the pigment epithelium, choroid and retina, except that in Parsons and Coats' case the defect was confined to the pigment epithelium only. Deyl held that his case supports the view of Lindsay Johnson, that colobomata are caused by choroidal naevi. Reviewing the cases of Bock, Deyl, Hess and Zimmermann, Ida Mann in 1926 concluded that they present evidence in favour of macular coloboma being due to intra-uterine inflammation—a reading that is not warranted either by the validity of the material or the findings reported.

Case Report.—The patient from whom the eye here described was removed, was a man aged 52 years, seen when unconscious and dying from cerebral thrombosis. The right eye was emmetropic and normal; the left was myopic to about 6 dioptres and showed a typical non-pigmented macular coloboma excavated

to at least 20 D. There were no changes associated with myopia apart from a small temporal crescent, separated by healthy tissue from the macular coloboma; the condition was distinctly a macular coloboma and not a generalised staphyloma posticum verum.

The eye was excised *in toto* and hardened in formalin. There was a distinct bulging of the sclera in the macular region, this bulging area being clearly separated by a normally shaped sclera extending to the disc (Fig. 1).

Histological examination.—From the point of view of discussion of the aetiological factors concerned in the condition of macular colobomata the histological picture is somewhat disappointing since the changes present are so extensive as to make it difficult to base suggestions concerning aetiology on them.

Of the coats in the region of the coloboma the choroid shows the most marked and the retina the least marked changes. Scleral changes whilst prominent do not compare with those seen in the choroid.

In the area corresponding with the region of greatest bulging the choroid is represented by a thinned stratum of connective tissue devoid of blood vessels and showing pigment in small amount only. This avascular zone appears to be limited to a

Wet specimen of eyeball.

small area measuring some 3-4 mm. only. Elsewhere, however, the choroid shows marked changes: blood vessels are few in number but extremely large and distorted appearing as flattened channels rather than tubular structures: the choriocapillaris is almost entirely deficient throughout. Pigment, whilst present, is deficient and irregularly distributed.

The retina shows secondary changes only from distortion of the globe and the condition of the optic nerve. Actually it is rather surprisingly well preserved.

The sclera, on the other hand, shares with the choroid, though to a lesser degree, histological changes which are very marked. Almost throughout, but most marked posteriorly, is a generalised ectasia: the fixed cells of the sclera are virtually absent so that the whole structure appears almost non-nucleated. Elastic tissue is present in small amount only, and for the most part the scleral coat is made up of collagenous fibrils. The episclera appears normal.

The optic nerve shows a complete lack of nerve fibres, degeneration being complete.

The changes described in this case, whilst similar in many respects to those met with in the case of the typical choroidal colobomata, show also a completely avascular zone corresponding with the position of the macular region. Moreover, the retina is less affected in the present instance than it would be with so extensive a choroidal coloboma of the typical variety.

So far as inferences are justified from the histological examination of this specimen it would appear probable that the condition is one associated with defective vascularisation rather than with any changes of a purely inflammatory character.

Discussion.

The older views on the causation of macular coloboma can be dismissed briefly as they have been dealt with by Parsons in 1906 and by Ida Mann in 1927, whilst the arguments in favour of secondary fissures as the cause of a typical coloboma have been reviewed recently by Rones.

(1) Developmental failures.—One view was the attempt to link up macular coloboma with typical choroidal coloboma by assuming that the macula is developed in the choroidal cleft which by rotation comes to lie horizontally. Apart from the fact that embryologists no longer admit this theory of rotation, the existence of both macular coloboma and typical choroidal coloboma in the same eye (cases of Wood and of Horton) invalidates this argument.

Other embryological theories postulate localised failure in the neural ectoderm, or in the pigment layer, as also abnormal development of the mesoderm. Treacher Collins implicated localised absence of posterior ciliary vessels, thus regarding colobomata as localised choroideremia.

(2) Inflammation.—That some macular " colobomata " are of post-natal origin cannot be doubted. The tuberculous nature of some of these lesions has been demonstrated by Funccius, by Meisner and by Harrison Butler amongst others. It is argued that intra-uterine inflammation explains the others. Ida Mann holds the pigmented coloboma to represent irritative and the non-pigmented destructive lesions.

(3) Trauma.—Trauma is a factor in macular changes that are hardly distinguishable from colobomata. The cases of Lagrange and the illustrations in Würdemann can be instanced. That birth injuries and haemorrhage are the cause was suggested by a number of observers.

(4) Naevus formation.—Lindsay Johnson held that typical colobomata represent choroidal naevi in varying stages of shrinkage. The indented edge and lobulated appearance of some lesions he held to be evidence in support of this view. As already mentioned Deyl held that the histological appearances in his case supported Johnson's theory. More recently this view has been upheld by Hoeg.

None of these theories is free from serious objection, Treacher Collins' view probably being the least unsatisfactory. The hereditary nature of macular coloboma militates against such factors as inflammation and trauma, whilst the association of skeletal defects with macular coloboma as a familial affection reported previously (Sorsby, 1935) suggests a mesodermal origin for coloboma. As far as it goes the histological evidence does not contradict the conception of Treacher Collins of macular coloboma as a localised choroideremia. This conception though it does not help to explain some of the features of macular coloboma—such as the presence of pigment in some cases and its absence in others, to mention only one—is of value not only because it represents an actual ophthalmoscopic observation, but also for the reason that it helps to link central colobomata with colobomata situated elsewhere outside the choroidal cleft. Furthermore, the absence of a scotoma in some of the cases of macular coloboma is best explained by invoking a lesion which affects the retina only secondarily and to a variable degree.

The view that macular colobomata are the result of defective localised vascularisation gains some support from the cases of familial central choroidal angio-sclerosis recently published in this

Journal (Sorsby, 1939). The fundi in two brothers whose eye trouble dated back to the early twenties showed a sharply-circumscribed central area in which the choroidal vessels were sclerosed. It is suggested that these cases of choroidal sclerosis are allied to macular coloboma—coloboma on the one hand and " senile " macular degeneration due to choroidal sclerosis on the other, representing the two extremes of a continuous range of dystrophy in which the two cases of central choroidal sclerosis with onset in early life form a connecting link.

Our thanks are due to Dr. A. D. Morris, Medical Superintendent of St. Leonard's (L.C.C.) Hospital and to Dr. K. S. May for the trouble they have taken to obtain the eye for examination.

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THE OPHTHALMOLOGICAL COMPLICATIONS OF LEONTIASIS OSSEA

BY

SEYMOUR PHILPS

LONDON

LEONTIASIS was the name given to certain forms of leprosy of the face, in which disease the thickened, seamed lips give the appearance of a lion's muzzle. In 1896, the name " leontiasis ossea " was coined by Virchow to describe a group of diseases which cause hyperostosis of the skull and facial bones. Specimens in many museums showed what different shapes these skulls might assume, but it was not until 1923 that any classification was attempted. In that year, Mr. Lawford Knaggs published an article in the *British Journal of Surgery* which is still the final word on the subject, and it is from that article that much of the information and three of the pictures reproduced here are obtained.

It is now clear that there are two types of hyperostosis:—

1. Creeping periostitis of the bones of the face and skull.
2. Diffuse osteitis of the bones of the face and skull.

a. General. *b*. Circumscribed. *c*. Local.

Creeping periostitis of the bones of the face and skull.—This condition most commonly affects the bones of the lower jaw, and has its origin from an infected tooth. It is possible for it to spread from the lower jaw over the bones of the face and cranial vault, leaving exuberant masses of compact bone in its path, which masses are densely opaque to X-rays, and of an ivory hard consistence. The ophthalmological interest of this type lies in the fact that in several instances it has started at the inner aspect of one or both orbits as a result of suppuration in the lacrimal sac. Virchow quotes the following case:—

A boy of twelve, the son of a surgeon named Fourcade at Perpignan, had a tumour of the right lacrimal sac which was opened by his father. It continued to suppurate for a very long time, and a bony tumour arose from the nasal portion of the right superior maxilla, which at the age of fifteen years compressed the right side of his nose so that it was difficult for him to breathe. It spread over both sides of his face until, five years

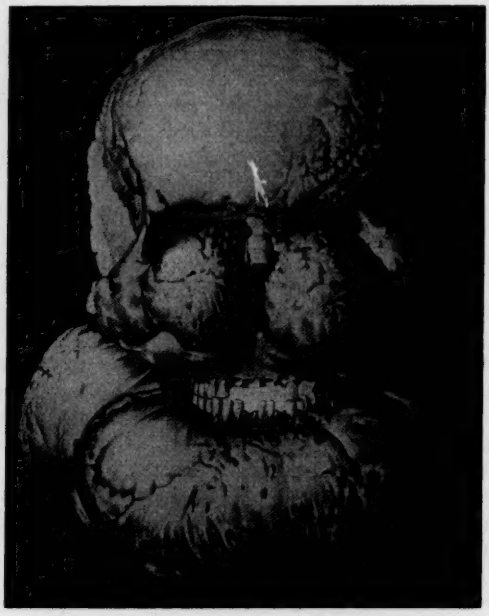

FIG. 1.

Fourcade's case. By kind permission of R. Lawford Knaggs.

later, " the face was monstrous and there was exophthalmos, myopia, and difficulty in speaking." He died, blind and phthisical at the age of forty-five and a picture of the skull will be seen in Fig. 1.

Another instance of this type of tumour is given by John Howship (Observations in Surgery, 1819). Howship examined a man who was then sixty years old, and goes on to tell how :—

" About fourteen years back he was walking up Hampstead Hill on a windy day, when he was attacked by a violent itching and heat in both his eyes. Before he could reach home he was unable to open his eyes in the light. Inflammation supervened, and a small tumour formed just below the inner angle of each eye, about the size of a hazel nut. These swellings burst inwardly, discharging freely between the eyelids. The inflammation was treated with poppy heads and fomentations, and went on for about twelve weeks, after which it subsided and he was able to go to work. A fortnight later he took a fresh cold, and on this occasion he applied to an eminent oculist, Mr. Ware, who ordered him to lay a warm poultice over each eye, as the swellings were again returning. About six weeks later both abscesses burst upon the cheek. The formation of these abscesses was attended with pain in the head the severity of which he could compare to nothing but the sensation of his head splitting asunder. For three months he was never free from the most insupportable and horrid pains in and about his head. He was advised to go into St. Bartholomew's Hospital, where he remained six weeks without anything material having been done. An operation had been proposed to him, which he did not choose to submit to, and he was consequently discharged from the House. There was now a considerable projection of tumour, apparently ossific, below the inferior margin of each orbit, the eyes being rendered more prominent than they are naturally.

The case excited much attention while in hospital, and one day one of the young gentlemen, observing the right eye, thrust out from the orbit, on pushing back the eyelid the globe of the eye suddenly sprung out beyond the palpebrae, and it was with some difficulty reduced again. At this time he had the power of perceiving light with the right but more with the left eye. He was often very delirious, and was subsequently informed that it was sometimes with extreme difficulty that he was prevented from tearing his eyes out in the rage of pain and delirium. In the course of an attack, the right eye burst from the intensity of the inflammation. The contents of the eyeball being effused, the excessive inflammation declined, and he became somewhat better. Sometime after his return home from hospital, he was putting down a turn-up bed, and not being able to see what he was about,

the bedstead slipped from his hand and fell, one of the feet striking him with great force upon the ball of the eye that was protruded, and lying upon the hard tumour in the cheek. By this accident the globe of the left eye was burst."

FIG. 2.

Howship's patient (after Howship).

In 1815 he remained well, but eventually died of an effusion of blood beneath the arachnoid. His skull may be seen in the Royal College of Surgeon's Museum, General Pathology Section, No. 1357.1 and Fig. 2, taken from Howship's book shows his appearance towards the end of his life.

Von Paas also describes a case of this type, and states that the pressure on the globes was such that one eye was destroyed, but the sight of the other had so far been preserved by trephining. This is the most recent case of this type that I can find in the literature, and think they are unlikely to occur at the present time, when lacrimal and other forms of suppuration are not allowed to continue for such long periods as in Howship's day. Should they occur, it is probable that the resources of modern surgery would prevent the disastrous consequences here described.

Diffuse Osteitis of the bones of the face and skull.—The bone in this disease presents a very different appearance from that which has just been described. There is no periosteal thickening, but the bone is expanded from within, and may reach a thickness of several inches. It is soft to cut and woolly in appearance, the X-ray picture being not unlike Paget's disease of bone.

A. *Generalised.*—Stack quoted one such case in which the skull had been growing for twenty years. None of the foramina was affected, and there was no interference with brain or nerve function. " The head was of enormous weight, so that the patient had been accustomed to sit supporting it with her hands, so that in time her forefingers were dislocated outwards by the burden."

John Greene (junior), in an excellent monograph on the subject, quoted a case which he saw first in 1907, and subsequently in 1914. He found marked improvement in the size of the skull during this time, the exophthalmos having receded to a remarkable extent, and the visual acuity remaining full, although latterly there was some optic atrophy and field loss.

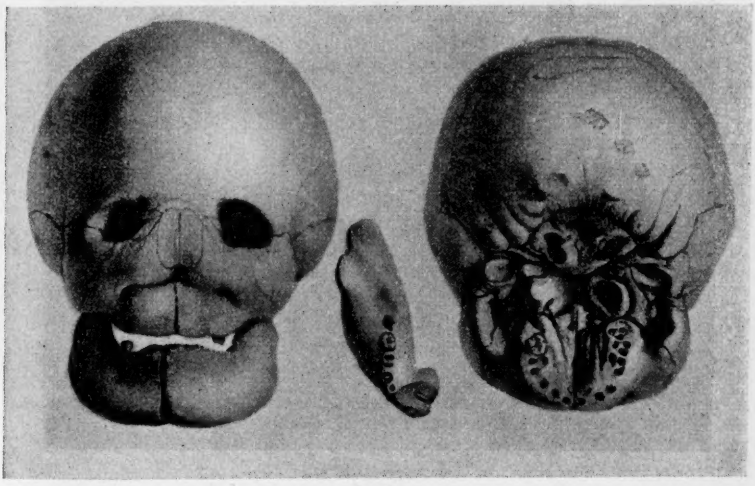

FIG. 3.

The Jadelot skull. By kind permission of R. Lawford Knaggs.

Fig. 3 is known as the Jadelot skull, and is that of a child of five. It shows the decrease in the size of the orbits, and consequent exophthalmos found in these patients. The skull was discovered

by accident, and no clinical history is available. The ophthalmological complications of this condition are therefore exophthalmos and myopia in the early stages, and optic atrophy in the later.

B. *Circumscribed Osteitis of one or more cranial bones.*—In spite of the very marked cranial and facial changes in this group,

FIG. 4.

H. M. P., aged 33 years. To show the downward displacement of the left orbit.

ophthalmological complications are not common, and when they occur do so only in the later stages.

H. M. P., aged 33 years, male, was seen by the author in

July, 1938, complaining of headaches. He had also noticed that the left side of his head was getting bigger.

History of the present condition.—The patient dated his troubles from a time fifteen years previously when he had suffered a motor accident, the top of the car coming down on his head. Examina-

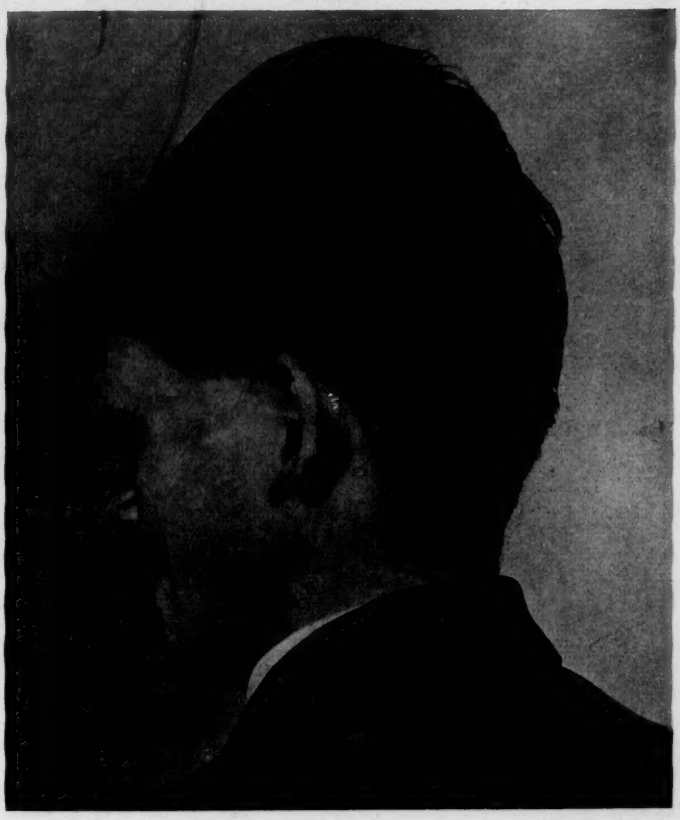

Fig. 5.

To show the overhanging brow. The large parietal exostosis has been covered over with hair.

tion of photographs taken eighteen years ago showed that there was marked bony deformity of the skull at that time, and thus the accident was probably in no way connected with the present condition.

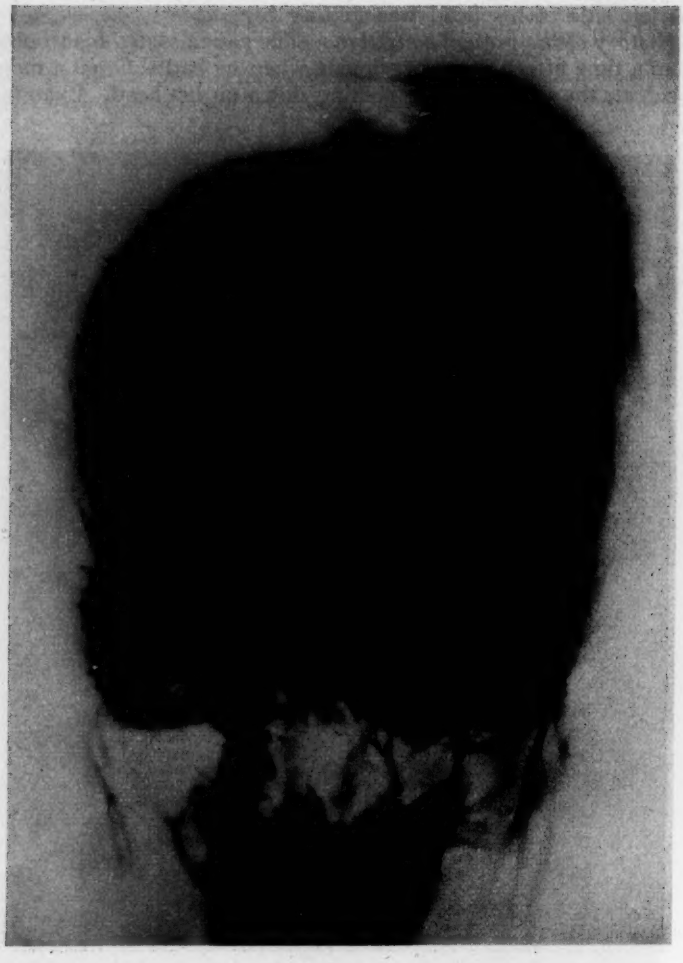

FIG. 6.

Showing the downward displacement of the left orbit and parietal exostosis.

Eleven years ago while in bed with 'flu, the doctor asked him what he had been doing to his head. This was the first reference he can remember to his condition, but it was very noticeable then and must have been present for many years before this.

Six years ago he was examined at a hospital for left-sided headaches, and although there was then a marked bony swelling of the vault of the skull, he cannot remember that any reference was made to it, and certainly no investigations were carried out.

For some years now, he has had to buy a bigger size in hats each year, and for the past nine months has worn none, as it was painful to do so. By July, 1938, he had found that his headaches were so bad that he could not carry on with his work,

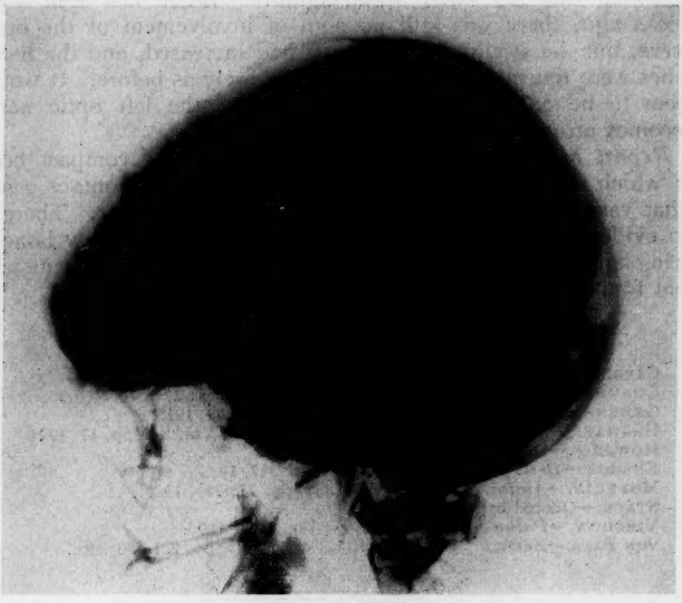

FIG. 7.

Lateral view of the skull. The filling in of the sphenoidal and other air sinuses is a characteristic of the disease.

and, as is so often the case with bony tumours, the pains troubled him chiefly at night.

Examination. There was a bony mass occupying the left parieto-occipital area, and also some thickening of the left frontal bone. This had caused the left orbit to be displaced downwards. The left eye was fifteen degrees convergent but all movements were full, the vision 6/6, and the visual field normal. There was no proptosis, and no abnormality of the fundus or media of the eye.

He was seen by Professor Paterson Ross, of St. Bartholomew's Hospital, who advised a linear osteotomy of the skull bones to relieve pain. This was done on August 22, 1938. The bone over the left parietal area was found to be between one and a half to two inches thick and very soft, but with no cysts. A longitudinal strip of bone half an inch wide was removed, and was followed by a marked improvement in the general condition of the patient, who was now free from headaches for the first time for a year. However, two months later he knocked his head, and following this his pains began again. When last seen some weeks ago, there was still no sign of involvement of the optic nerve, but the swelling of the head had increased, and the headaches were returning, though not so severely as before. It would seem to be only a matter of time before the left optic nerve becomes atrophic.

Report on bone removed. The sections show compact bone in which the Haversian canals are enlarged and contain somewhat vascular fibrous tissue which is almost acellular. There is no evidence of lacunar resorption of bone, and no new bone is being laid down. The appearance of the bone is consistent with that found in osteitis fibrosa.

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CULTURE IN VITRO OF THE CORPUSCLES OF TRACHOMA

BY

DR. L. POLEFF

INSTITUT D'HYGIENE DU MAROC

IN his comprehensive report on the aetiology of trachoma MacCallan concludes that the causal agent of this infection is certainly a virus. The group of minute organisms to which it belongs is characterized by the following features: (1) The formation of intracellular inclusions in the tissues affected by the

EXPLANATION OF FIGURES

ORIGIN : Cellular culture of trachomatous conjunctiva (series 23) in which the films showed only very few Rickettsia-like bodies (elementary bodies), and absence of inclusions.

INCUBATION: 10 days. STAINING with Castaneda-Lepine. MAGNIFICATION ×1000

FIG. 1.

Epithelial cell crammed with elementary bodies. Classical appearance.

FIG. 2.

Voluminous inclusions consisting of initial bodies in process of division.

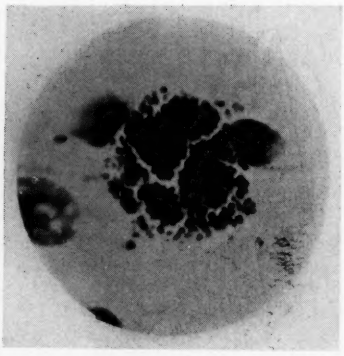

FIG. 3.

Epithelial cell which has just burst full of mulberry-like inclusions.

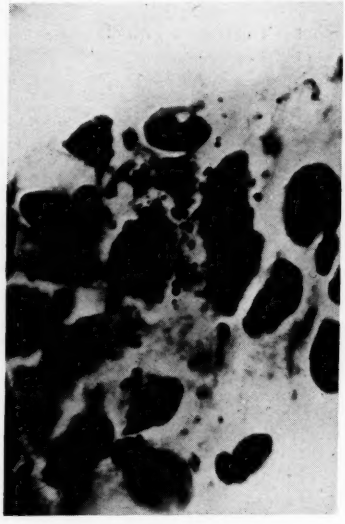

FIG. 4.

Free initial and elementary bodies.

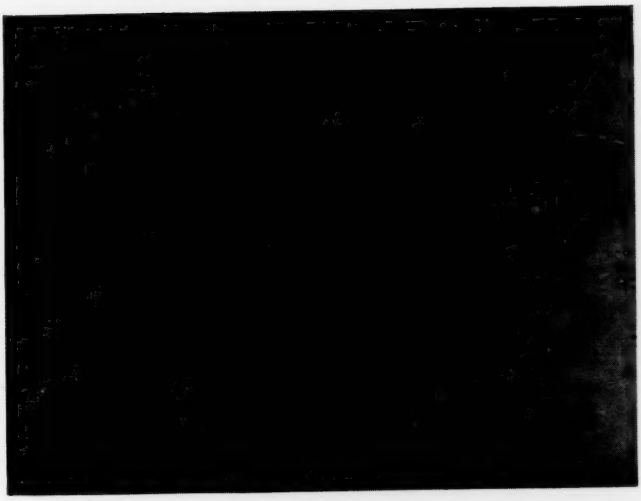

FIG. 5.

Elementary bodies in an epithelial cell from a trachomatous conjunctiva.

NOTE BY TRANSLATOR

Dr. Poleff published his first account of the tissue-culture of trachoma in 1936 (*Arch. d'Ophtal.*, p. 882). He has found the best culture media to be the human placenta and the human corneal tissue. The microphotographs which illustrate his paper are what he believes to be the aetiological agent of trachoma in several phases of development obtained from tissue cultures. For purposes of comparison a microphotograph of a human epithelial cell from the conjunctiva of a trachomatous person is included, showing elementary bodies: magnification ×2000; taken at Westminster Hospital Research Laboratories.

pathological process and which present a certain stage in the evolution of the causative agent. (2) Filterability of the primitive elements (elementary bodies) of the virus through porcelain filters, through which ordinary bacteria cannot pass. (3) Obligatory parasitism, that is to say development *in vitro* occurs only in the presence of living cells.

The intracellular inclusions of trachoma were discovered in 1907 by Halberstaedter and Prowaczek, as everyone knows. Already before the world war Axenfeld in his classical work on the aetiology of trachoma asserted their importance, and this has been emphasized more recently by Thygeson and his co-workers, by Julianelle and Harrison, as well as more particularly by the recent work of Foley and Parrot (*Arch. Inst. Pasteur d'Algerie,* Vols. XV, XVI).

The filterability of trachoma virus was established by Nicolle, Cuénod and Blaizot in 1912, and has recently been confirmed by Thygeson.

I have shown the relationship which exists between the smallest forms of the virus (elementary bodies) and the intracellular inclusions by cellular cultures of trachoma; this was carried out on more than ten thousand films and sections prepared from these cultures, and from these, studies have been made as to the stages of development, and their living nature has been proved. Proof of vitality, which can only be obtained on appropriate living tissue, is an important if not decisive argument in favour of the aetiological specificity of inclusions and their derivatives in trachoma.

In view of the uncertainty which exists as to the culture of the trachomatous corpuscles I present to this Meeting of the International Organization against Trachoma a series of microphotographs which exhibit typical pictures of the various stages of their evolution *in vitro*. In the original preparations, of which these are photographs, the corpuscles appear in such a fashion that I can now have no doubt as to their parasitic nature. According to their cycle of evolution observed *in vitro,* which corresponds in general with the results obtained by myself and many others on fresh trachomatous tissue, these parasitic atoms probably belong to the class of *ultraviruses,* but their exact biomorphological classification, virus or Rickettsia, seems to be uncertain. In German and English literature they are described as elementary bodies (virus-forming inclusions). Busacca was the first to suggest that the virus of trachoma belonged to the Rickettsiae and had nothing to do with the epithelial inclusions of Halberstaedter and Prowaczek.

However this conception of Busacca is accepted by no one. My

own observations have always led me to conclude that the Rickettsia-like corpuscles described by Busacca, and later by Cuénod, at any rate those which are not debris, cellular and other, are identical with the inclusion of Halberstaedter and Prowaczek at certain stages of their evolution.

At the present time most trachomatologists believe that we are concerned with a single minute infecting agent, which has characters both of a virus and of a Rickettsia. The culture of this element *in vitro* and the inoculation of susceptible animals, and man also, may allow a precise definition to be made.

ANNOTATION

November 1st, 1914 : 1939

Five and twenty years ago to the day the Germans were responsible for a piece of atrocity of a particularly uncivilised nature. We refer to the deliberate murder of Angus McNab while engaged in giving first-aid to wounded London Scottish after the charge at Messines.

It was bright moonlight at the time; McNab, himself wounded, was unarmed and wearing the Red-cross badge. In short it was entirely unjustified.

McNab spoke German fluently, had worked in Axenfeld's clinic at Freiburg and was a great admirer of German clinical and laboratory methods. It was one of the ironies of fate that he should have lost his life thus at the hands of the nation he so much admired.

Twenty-five years later the British Empire is again at war with Germany, and even in these early days of the war the same uncivilised methods are again in evidence.

ABSTRACTS

I.—RETINA

(1) **Kurz, Otto (Prague).—The clinical features and pathogenesis of non-myopic detachments of the retina. (Zur Klinik und Pathogenese der nichtmyopischen Netzhautabhebungen—starre Abhebung, Netzhautcysten, Netzhautspaltung).** *Arch. f. Ophthal.*, Vol. CXXXIX, p. 326.

(1) **Kurz** here deals with forms of detachment in which retinal tears do not form the most prominent feature—rigid detachments, retinal cysts and splitting of the retina.

The rigid detachments are grouped according to their origin:—(1) trauma, contusions with disinsertion; (2) the presence of exudative changes, either visible in the eye (choroiditis) or probable owing to the general condition (tuberculosis, vaso-neurosis, allergy); (3) all other cases, and of these those showing disinsertions are regarded as of inflammatory origin rather than due to cysts.

A review of the cases of cyst formation indicates differences in their clinical character and causation (probable congenital defect in the retina, exudative processes, tumour, trauma).

Splitting of the retina, retinoschisis, into two or more layers arises from cystoid degeneration of the retina, the vacuoles, which may appear at different levels in the retina, increasing in size and coalescing to form cysts. If the degeneration progresses radially the retinal layers tend to become thinned through pressure by the vacuoles and rupture, such tears producing different clinical forms of retinochisis according as they involve all the layers of the retina or only the external layer. The site of such a rupture after operative reposition of the retina may be recognised by its homogeneous pigmentation.

THOS. SNOWBALL.

II.—CORNEA

(1) **Berardi and Motolese (Florence).—Familial corneal dystrophy. (Distrofia corneale familiare con disepiteliazzioni recidivanti).** *Boll. d'Ocul.*, September, 1938.

(1) Degeneration of the cornea takes many forms and is markedly hereditary. The authors record a family who show an irregular form of degeneration of the cornea, complicated in some individuals by loss of the underlying epithelium. Thirteen relatives were seen and of these nine were affected. The history of others seemed to show them to have escaped the taint, but since in some of those examined the changes were visible only to careful examination, they were not necessarily immune. Three were known to be affected.

HAROLD GRIMSDALE.

(2) **Bücklers, M. (Tubingen).—Droplets on the corneal epithelium in furniture workers. (Tröpfchenförmige Niederschläge auf der Hornhautoberfläche bei Möbelarbeitern).** *Klin. Monatsbl. f. Augenheilk.*, Vol. XCIX, p. 676, 1937.

(2) **Bücklers** describes a complaint of lacquer polishers using a lacquer spray who suffer from irritable and painful eyes. On

examination they are found to have clear deposits of lacquer on the corneal epithelium—the latter can only be seen by reflected light in the slit-lamp and under great magnification, so that it is easy to mistake the condition for an ordinary conjunctivitis. In contrast to the severity of the symptoms the eyes are little inflamed. Only a small percentage of workers are affected and more in the winter months when probably lack of ventilation causes the atmosphere to be more saturated with lacquer solution.

D. R. CAMPBELL.

III.—MISCELLANEOUS

(1) **Harrison Butler, T. (Birmingham).—Some modern advances in ophthalmology.** *Birmingham Med. Rev.*, March, 1939.

(1) This short paper is an abridged record of **Harrison Butler's** Presidential Address to the Birmingham Branch of the British Medical Association. Its actual title was "A Pictorial Demonstration of modern advances in Ophthalmology" and it was illustrated by a wealth of the author's own drawings. Of these there are printed on four full pages the number of 17 illustrations, including a reproduction of the slit-lamp and corneal microscope and a diagram showing the various methods of illumination. Judging from the abridgement the lecture must have been an admirable survey of the things that can be seen with the slit-lamp and particularly well suited to the needs of a general medical audience.

R. R. J.

(2) **Döhmen, H. (Frankfurt).—Bacteriological and chemical investigation of the prevention and treatment of ocular infection. (Bakteriologische und chemische Untersuchungen zur Verhutung und Behandlung von Infektionen am Auge).** *Klin. Monatsbl. f. Augenheilk.*, Vol. CI, p. 515, 1938.

(2) **Döhmen** investigated the bactericidal action of various antiseptics and found that optochin was most effective against pneumococci, and acridin dye against streptococci and staphylococci. A combination of these in oily solution—biseptol simplex (Winzer-Konstanz) proved an excellent antiseptic in cases of perforating injury and acute corneal infection, as well as in experimentally-produced ulcers in rabbits. The combination of biseptol with a new derivative of cocaine—psicain-neu—in the form of biseptol co. was also a very efficacious remedy.

D. R. CAMPBELL.

(3) **Heinsius, E. (Kiel-Wik).—The "simple, uncomplicated" form of congenital total colour-blindness. (Die "einfache unkomplizierte" Form der angeborenen totalen Farbenblindheit).** *Klin. Monatsbl. f. Augenheilk.*, Vol. CI, p. 489, 1938.

(3) **Heinsius** reports a case of total colour blindness in a boy of 19 years, who had good central visual acuity and a normal curve for dark adaptation. He considers that these two factors negative the theory that total colour blindness is due to defective cone-function and suggests that some higher (cerebral) centre is at fault. He was unable to trace any family history of defective colour-vision.

D. R. CAMPBELL.

BOOK NOTICES

Clio Medica: Ophthalmology. By BURTON CHANCE, M.D. Pp. 240, with 6 illustrations. Paul B. Hoeber, Inc. Medical Book Department of Harper and Brothers. New York. 1939. Price, 2 dollars.

Clio Medica consists of a series of primers on the history of medicine under the editorship of Dr. E. B. Krumbhaar. The XXth of the series is a primer of the history of ophthalmology by Dr. Burton Chance, whose work in ophthalmology and in medical history has gained him a well deserved reputation which extends far beyond the boundaries of the United States. This book consists of 26 chapters for the most part arranged on a chronological basis. It is remarkably complete and very well done. The earlier chapters are on Sumerian, Babylonian and Assyrian; Egyptian; Chinese; Graeco-Roman and Arabian ophthalmology. Then follow chapters on ophthalmology in Salerno and the West; discoveries in the 16th century; anatomical and physical advances in the 17th century; cataract in the 18th century; and modern period.

The latter part of the book is given to chapters on 19th century scientific developments; sympathetic ophthalmitis and focal disease; refraction and spectacles; co-ordination of eye movements; blepharoplastic surgery; colour vision and colour blindness; atropine and other drugs; ophthalmic surgery; therapeutic agents; hospitals and teachers; pathology of the eye; societies and journals; modern British contributors; ophthalmology in America; prevention of blindness, the care and education of the blind; and conclusion.

It will be seen that the author has spread his net widely and has touched on every aspect of ophthalmological history. All is good and the student for whom these primers have been written will find

here a thoroughly reliable guide to the subject. The reviewer has read with the greatest interest the chapters on ophthalmology in America and on the prevention of blindness and care and education of the blind, subjects in which America has done pioneer work.

The kindly notice of Dr. Harlan, of Philadelphia (1835-1909), shows the author's gratitude to one of his predecessors.

We noticed very few errors but Dr. Burton Chance seems to have fallen into one over the *Ophthalmic Review* "which had only a short lived existence and was founded in 1882." He is thinking of the first *Ophthalmic Review*, in three volumes, founded by Laurence and Windsor in 1864. The second *Ophthalmic Review*, founded in 1882 by Priestley Smith and Karl Grossmann, ran to 35 volumes and was merged in the *British Journal of Ophthalmology* in 1917. The discovery of Richard Banister's description of the hardness of the eyeball in glaucoma is here attributed to James, but it is really due to Arnold Sorsby. But, we will not make too much of these trifling errors and the reviewer can honestly say that the reading of Dr. Burton Chance's book during these dark days has been a joy for which he is most grateful.

The book is well printed, the illustrations, though few in number, have been admirably chosen and reproduced and a special word of praise is due to the very complete index.

NOTES

Appointment

EDWARD BACON has been appointed Hon. Assistant Ophthalmic Surgeon to the Southampton Free Eye Hospital.

* * * *

Royal Westminster Ophthalmic Hospital

WE are asked to state that the Royal Westminster Ophthalmic Hospital will resume its usual activities, as regards classes and teaching, at the earliest possible moment.

FUTURE ARRANGEMENTS

1940

July 4-6.—Ophthalmological Congress, at Oxford.